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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STANDLEY, STEVEN H	
ART UNIT	**PAPER NUMBER**
1649	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/508,343	VON DER KAMMER ET AL.	
	Examiner	Art Unit	
	Steven H. Standley	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 21-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group 23, claims 18-20, in the reply filed on 7/17/07 is acknowledged.

Claims 18-20 are under consideration.

Priority

2. This application claims priority to US provisional 60/365,815 filed 3/21/02.

Information Disclosure Statement

3. The IDS dated 4/06 has been considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an assay for screening ***candidate*** compounds for neurodegenerative diseases in particular Alzheimer's, does not reasonably provide enablement for an assay for screening for "a modulator of neurodegenerative diseases," in particular "Alzheimer's disease." Or related diseases or disorders or one or more substances selected from the group consisting of...". The specification does not enable

any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to:

1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The invention is a method of screening for modulators of neurodegenerative diseases by contacting a cell with a test compound and measuring activity or level of expression of various forms of Maguin. It is complex because it is not known whether or if Maguin-1 or Maguin –2 protein or RNA has any relationship to generic "neurodegenerative diseases" or Alzheimer's disease (AD) in particular, other than the mRNA is more highly expressed in AD brains than controls.

The state of the prior art is that Maguin, Membrane-associated guanylate kinase interacting protein, has no known role in any neurodegenerative diseases. Moreover, the post-filing date art recognizes no link between Maguin-1 or 2 and neurodegenerative diseases. The prior art only recognizes Maguin functionally as a protein that binds some proteins that are localized subjacent to the postsynaptic membrane in synapses, such as PSD-95 (see Yao et al. 1999). Since the function of Maguin proteins is largely

unknown, and Maguin has no relationship to neurodegenerative diseases in the prior art, the role of Maguin in neurodegenerative diseases and in Alzheimer's disease is entirely unpredictable.

The specification provides differential display pcr done with normal brain compared to AD and finds Maguin mRNA somewhat elevated in AD compared to control. However, the specification lacks teaching or guidance as to whether a compound that modifies the activity or expression level of Maguin will necessarily modulate neurodegenerative diseases or AD.

Therefore, given the lack of support in the prior art, the lack of predictability of a role in neurodegenerative diseases, the lack of support or guidance as to whether a compound that modifies the activity or expression of Maguins would modulate neurodegenerative diseases, it would require undue experimentation to use the invention commensurate with the scope of the claims.

5. Claims 18-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

. The claims are drawn to a method of identifying compounds that bind the maguin-1 and maguin-2 polypeptides, or fragments or derivatives or variants. The claims do not require that the polypeptides possess any particular biological activity except binding to

eachother, nor any particular conserved structure, or other disclosed distinguishing feature. Therefore, there are no clear structural limitations on the complex of polypeptides claimed. Thus, the claims are drawn to a genus of polypeptides that constitute an single amino acid or more as a 'maguin' fragment, or variant or derivative. Moreover, there is no written description as to what constitutes 'activity' in the claimed method. Also, the term 'ligand' is limited to the PSD-95. One skilled in the art would not recognize a 'ligand' for Maguin-1 and 2.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. In the instant application, no such distinctions have been made.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the

method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only polypeptides comprising the amino acid sequence set forth in the SEQ ID NO: 1 and 2 (which encode maguin-1 and 2), but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

What is the activity measured in claim 18? What is the "ligand" used in claim 19? Have they described any activity or ligand?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claim 18 rejected under 35 U.S.C. 102(b) as being anticipated by Donello et al (2001).

The specification defines "fragment" in the following manner: "The term "fragment" as used herein is meant to comprise e.g. an alternatively spliced, or truncated, or otherwise cleaved transcription product or translation products [page 6-7, spec]." The broadest reasonable interpretation of "truncation" or "cleaved translation products" is a single amino acid fragment. Donello et al. contact a cell with an alpha-2 agonist (i.e., test compound) and measuring the level of extracellular glutamate (i.e., the maguin-1 fragment) and comparing it to a control (see, for instance, figure 5a wherein a saline-treated cell is compared to agonist-treated cell. The examiner has given no patentable weight to the preamble, "an assay for screening for a modulator of neurodegenerative diseases...." A preamble which describes intended use is given no patentable weight by the examiner. See In re Hirao, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and Kropa v. Robie, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

7. Claim 20 rejected under 35 U.S.C. 102(b) as being anticipated by Yao et al (1999).

Yao et al disclose a method of testing a compound to determine if said compound binds to Maguin-1 or 2 wherein a liquid suspension of maguin 1 and 2 is added (See Figure 5, section B), a detectable compound is added (see mcy-PSD-95

PDZ domains), the solution is incubated and amounts of the detectable compound are measured (see Western blot) and the degree of binding is determined (compare lane 4 to lanes 5 and 6; a decrease indicated binding).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yao et al (1999) as applied above, and in further view of Tao et al (US patent publication 2002/0045590 A1, filed may 2001 with priority to provisional application 60/242,580).

Yao et al disclose Maguin-1 and Maguin-2 proteins (see Figure 1, page 11890) and identify two proteins that bind Maguin-1 and 2: S-SCAM and PSD-95. Yao et al identifies the expression patterns, subcellular distribution, expression levels, and compounds (ie, proteins) that bind to Maguin-1. In particular, Yao et al demonstrate that Maguin-1 binds specifically to the 3 PDZ domains of PSD-95 (see Figure 5, B, rows 4-6) via it's C-terminal PDZ-domain binding motif (see abstract), which is the same binding motif and interaction as is NMDA receptors and PSD-95.

Yao et al dose not disclose an assay to identify compounds that interfere with binding between maguin and a 'ligand,' and do not teach an assay to identify compounds that affect expression or activity.

Tao et al disclose an assay to identify compounds that interfere with the binding of NMDA receptor c-terminus and the PDZ domains of PSD-95, and with nNOS and the PDZ domains of PSD-95. Moreover, Tao et al disclose a preferable method of identifying compounds that bind the PDZ domains of PSD-95 and inhibit binding of NMDA receptors or nNOS (see [0026]). Thus, Tao teaches all the steps of claim 19. In particular, see section 0016. Moreover, the assay of Tao is commonly carried out in a liquid suspension. Tao et al. also disclose contacting a cell with a test compound (psd-95 antisense polynucleotides; see example 2, page 5) and measuring the expression of PSD-95.

It would be obvious to use the assays of Tao et al with the Maguin protein of Yao et al **because NMDA, nNOS, and Maguin bind the same PDZ domains in PSD-95 via the same PDZ-binding domain interaction with the PDZ domains of PSD-95.**

Thus, an assay to identify compounds that interfere with Maguin-1-PSD-95 binding would identify compounds that would also inhibit binding of NMDA receptors to PSD-95 and nNOS to PSD-95.

One would be motivated to combine the PSD-95 binding protein Maguin of Yao et al with the assays of Tao et al because compounds that inhibit binding to the PDZ binding domains of PSD-95 would be useful to treat pain, as disclosed by Tao et al. (see [0011]). One would also be motivated to measure the expression of Maguin after contacting a cell with a compound because Maguin binds PSD-95, and would modulate association of NMDA receptors and/or nNOS with PSD-95 since they share the same binding site.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven Standley whose telephone number is **(571) 272-3432**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on **(571) 272-0841**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Steve Standley, Ph.D.
9/17/07

DAVID S. ROMEO
PRIMARY EXAMINER